1631

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of	) Examiner: Lori A. Clow
Gerard Grassy et al.	) Art Unit: 1631
Serial No. 09/359,181	)
Filed: July 22, 1999	)
For: "Computer-Aided Method for the Provision, Identification, and Description of Molecules Capable of Exhibiting a Desired Behavior, More Particularly in the Pharmaceutical Sector, and Molecules Obtained by Said Method"	)

Certificate of Mailing Under 37 C.F.R. §1.8(a):

I hereby certify that this correspondence is being deposited on May 4, 2004 with the United States Postal Service as first-class mail in an envelope properly addressed to the Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

May 4, 2004
Date of Certificate

Robin Dolan

REQUEST FOR RECONSIDERATION UNDER 37 C.F.R. §1.111

The February 4, 2004 Official Action has been carefully reviewed. In view of the following remarks, favorable reconsideration and allowance of this application are respectfully requested.

The Examiner has rejected claims 1, 4, 5, 8-10, 18-20, and 73 for allegedly failing to satisfy the written description and enablement requirements under 35 U.S.C. §112, first paragraph.

Claims 1, 4, 5, 8-10, 18-20, and 73 have also been rejected by the Examiner under 35 U.S.C. §112, second

paragraph for alleged indefiniteness.

The foregoing rejections constitute all of the grounds set forth in the February 4, 2004 Official Action for refusing the present application.

CLAIMS 1, 4, 5, 8-10, 18-20, AND 73 SATISFY THE WRITTEN DESCRIPTION REQUIREMENTS UNDER 35 U.S.C. §112, FIRST PARAGRAPH

The Examiner has rejected claims 1, 4, 5, 8-10, 18-20, and 73 for allegedly failing to satisfy the written description requirements under 35 U.S.C. §112, first paragraph.

Specifically, the Examiner contends, at pages 2-3 of the instant Office Action, that "there is **no** description of the 'dynamic filter'" (emphasis added) in the specification. Applicants respectfully disagree with the Examiner's contention. As noted in the Official Action response dated September 30, 2003 (see specifically pages 6-9), the passages from page 9, line 3 to page 10 line 22 and page 35, line 3 to page 37 line 23 of the instant application describe a dynamic filter. Indeed, the Examiner, at page 7 of the instant Official Action, notes that the "specification gives one example of a dynamic filter as one based on conformational space of the molecule ... over time."

It is the Examiner's position, however, that the above-mentioned passages in the instant specification "merely describes components of a filter, such as Principal Component Analysis (PCA)." Applicants submit that a skilled artisan would readily be aware of the "particulars" of the dynamic filter. Indeed, the passage from page 8, line 20 to page 9, line 8 explains how a dynamic filter differs from a static filter; the passage at page 9, line 9 to page 10, line 22 describes in general terms the use of autocorrelation vectors in a dynamic filter; and the passage at page 35, line 10 to page 37 line 3 describes not only the components of a dynamic

filter, but how those components operate and interact in relation to a specific example.

The Examiner also contends that "it is generally considered that the terms 'dynamic' and 'filter' imply that change in response to some parameter is occurring and that selection for a desired outcome is made based upon or in response to the change." Thus, "dynamic" is defined as a "change in response to some parameter," and "filter" is defined as a "selection for a desired outcome based upon or in response to the change". It is the Examiner's position that there is "no description of these details in the specification." Without necessarily accepting the above-mentioned definitions of "dynamic" and "filter," Applicants submit hereinbelow that the allegedly absent details are, indeed, in the specification.

With regard to the term "dynamic," the specification at page 9, lines 10-12 explains that the dynamic filter may be based on "the variation in the space occupied by a molecule over a period of time." Comparing this with the Examiner's definition, the "change" equates to the variation in space occupied by the molecule (i.e. conformational variation) and this change is in response to the "parameter" of the passage of time. Further, the specification at page 9, lines 13-20 explains in general terms how molecular modeling and autocorrelation vectors can be used to determine and represent such variation. The specification at page 35, line 10 to page 37, line 3 describes in great detail a modeling approach based on molecular dynamics (MD) simulation which allows these vectors to be determined. Thus, the specification clearly provides a description of "change in response to some parameter," i.e. a "dynamic" condition.

As to the term "filter," the specification, at page 7, lines 1-5, states that "a molecule may be predicted to be active only if a certain descriptor value" is within the range of values set forth in the filter. Additionally, the

specification states that the:

> "method of designing molecules may include testing a plurality of candidate molecule to determine whether they conform to said derived criteria (i.e. have descriptor values within the range(s) associated with activity). That is, each of the criteria constitutes a 'filter' for testing candidate molecules" (page 8, lines 20-25).

It is clear throughout the specification (see, for example, page 9, lines 3-13) that the certain descriptor can be conformational variation. Thus, the specification discloses that the action of a filter is to predict/determine that a molecule is active when a conformational variation value is within a range. Comparing this with the Examiner's definition, the phrase "selection for a desired outcome" equates to the prediction/determination that a molecule is active, and the phrase "based upon or in response to the change" equates to the prediction/determination being made when the conformational variation value for the molecule is within a particular range.

Furthermore, the specification at page 9, line 21 to page 10, line 10 and page 37, lines 4-23 provides guidance as to how autocorrelation vectors representing conformational variation can be compared with a required range, wherein principal component analysis (PCA) was used to reduce the dimensions of the autocorrelation vector data set. In the example at page 35, line 10 to page 37, line 3, the required range is the conformational space range of four of the five peptides. These four peptides were all shown to be active *in vivo* whereas the fifth peptide, which exhibited a different conformational space, was shown to be inactive. Thus, the concept of a "filter" as a "selection for a desired outcome based upon or in response to the change" is clearly present in the specification.

Thus, contrary to the Examiner's objection, the specification clearly provides sufficient description of the terms "dynamic" and "filter."

Applicants also respectfully draw the Examiner's attention to the fact that independent claims 1 and 18 require a dynamic filter "representing constraints of conformational variations which each candidate molecule must satisfy in order to exhibit said immunomodulatory activity." Thus, the instantly claimed invention does not require a written description of all possible types of dynamic filters (which Applicants maintain the specification does provide), but rather only requires written description in support of dynamic filters which are directed to filtering for conformational variation constraints for the purpose of identifying molecules which exhibit immunomodulatory activity.

An adequate written description of a dynamic filter, which is directed to filtering for conformational variation constraints, is provided, for example, from page 35, line 10 through page 37, line 23. Furthermore, the Examiner, at page 7 of the instant Official Action, does indicate that the specification provides an "example of a dynamic filter." However, the Examiner contends that the dynamic filter is "based on conformational space of the molecule and ... that distances between inactive and active molecules are calculated over time and then represented in an autocorrelogram." Applicants disagree with the Examiner's interpretation of the dynamic filter. Indeed, at page 9, lines 13-18, the specification states that "for each molecule of a given set of active and inactive molecules an autocorrelation vector of interatomic distances may be calculated over a predefined period of time." Thus for the purpose of calculating the series of autocorrelation vectors for each molecule, the molecule is considered <u>separately</u> from the other molecules of the set, and the vector contains <u>interatomic</u> not intermolecular distances.

The Examiner also states, at page 7 of the instant Official Action, that it is "unclear from the description if the dynamic filter is responsible for selecting certain atomic

distances over time or all atomic distances over time." However, the specification states at page 36, lines 13 and 14 that the "distances between all pairs of atoms were calculated." Thus, with regard to the provided example, it is quite clear that all atomic distances over time were selected. Applicants submit, however, that the skilled artisan would realize that fewer distances could be selected and measured in order to lessen the computations required.

Lastly, the Examiner asserts that it is "not described how the dynamic filter is any different from the static filter." Applicants respectfully direct the Examiner attention to the passage at page 8, line 26 to page 9, line 8, which clearly explains that a static filter "employs one or more descriptors which characterize a molecule in a static or time averaged state," whereas a dynamic filter "employs one or more descriptors which characterize the dynamic behavior of a molecule." Thus, a filter employing a series of autocorrelation vectors, for example, is dynamic because the series of vectors describe how the conformation of the molecule develops over time. In contrast, a filter employing the descriptors listed in Table II is static because each descriptor relates to a time-invariant property.

In light of all of the foregoing remarks, Applicants respectfully request the rejection of claims 1, 4, 5, 8-10, 18-20, and 73 for allegedly failing to satisfy the written description requirement under 35 U.S.C. §112, first paragraph for be withdrawn.

CLAIMS 1, 4, 5, 8-10, 18-20, AND 73 SATISFY THE ENABLEMENT REQUIREMENTS UNDER 35 U.S.C. §112, FIRST PARAGRAPH

The Examiner has also rejected claims 1, 4, 5, 8-10, 18-20, and 73 for allegedly failing to satisfy the enablement requirements under 35 U.S.C. §112, first paragraph. It is the Examiner's position that undue experimentation would be required to make and use the invention as claimed.

Applicants respectfully disagree with the Examiner's interpretation of the instant application in light of the enablement factors set forth in In re Wands. The Examiner's position is discussed hereinbelow.

With respect to factors (b) the amount of direction or guidance presented and (c) the presence or absence of working examples, the Examiner only identifies the passage at page 17, lines 19-24 as providing direction or guidance on dynamic filtering, despite indicating at page 7 of the instant Official Action that Applicants have provided an "example of a dynamic filter." The passage at page 17, lines 19-24 merely points out that the Multidyn software **can** (not "must") be used to characterize the conformational spaces. Essentially the passage is supplemental to the passages at page 9, line 3 to page 10, line 22 and page 35, line 3 to page 37 line 23, which provide detailed guidance to performing a dynamic filtering step. Furthermore, the passage at page 17, lines 19-24 is not inconsistent with point 11e of the van de Waterbeemd declaration, as implied by the Examiner, because the declaration merely sets forth that the Multidyn software is **not essential** for the performance of dynamic filtering. Furthermore, the van de Waterbeemd declaration indicates that a skilled artisan would readily appreciate that the Multidyn software is "an example of a convenient platform" to analyze conformational spaces (point 11e).

Additionally, Han van de Waterbeemd, a highly respected and highly skilled artisan in the field of the claimed invention, in his submitted declaration clearly indicates that the "specific example at page 35, line 3 to page 37, line 23" of the instant application is "sufficient to enable any skilled artisan in the art to make and use the dynamic filters" of the instant invention (point 10). Han van de Waterbeemd also indicates that the dynamic filter is described in terms of three types of analyses (i.e. MD analysis, autocorrelograms, and PCA) that were known to a

skilled artisan at the time of the instant invention (point 11). Thus, Applicants respectfully submit that the presence of a working example in addition to adequate direction and guidance would fully enable a skilled artisan to make and use the claimed invention.

As to factors (e) the state of the prior art and (g) the predictability of the art, Applicants respectfully submit that the Examiner's argument appears to be founded on an alleged lack of a written description as opposed to a proper enablement analysis of the state and predictability of the field of the claimed invention. The Examiner notes, at page 5 of the instant Official Action, that the "specification merely describes components of the [dynamic] filter" and that the specification "does not provide a description of a dynamic filter" in a way that is analogous to the specification of three older U.S. patents cited by the Examiner pertaining to static filters. Applicants respectfully submit that the issues pertaining to the written description in support of "dynamic filtering" has been addressed hereinabove. However, to further address the Examiner's concerns, Applicants point out that Han van de Waterbeemd in his declaration indicated that the dynamic filter exemplified in the instant specification is described in terms of MD analysis, autocorrelograms, and PCA, all of which were known to the skilled artisan at the time of the instant invention. It is a well settled premise in patent law that a patent need not teach, and preferably omits what is well-known in the art. Lindemann Maschinenfabrik v. American Hoist and Derrick, 221 USPQ 481, 489 (Fed. Cir. 1984). Inasmuch as the components employed to describe the dynamic filter were known to a skilled artisan at the time of the invention, Applicants need not supply the detailed mathematical equations and algorithms behind these analyses as provided by the three U.S. patents cited by the Examiner.

Returning to the enablement analysis of (e) the state of the prior art and (g) the predictability of the art as well as (f) the relative skill of those in the art, Applicants submit that all three factors support a finding that the instant specification is fully enabling for the claimed invention. Indeed, the state of the prior art must be considered high because static filtering, as noted by the Examiner, was well known in the art and the three analyses employed to discuss dynamic filtering were all well-established as noted by the van de Waterbeemd declaration. Inasmuch as the technology is mathematically-driven and computer-based, the predictability of the art must be considered very high. Lastly, as evidenced by the generation of various software programs to perform the analyses described in the instant application, the relative skill of those in the art is high.

With regards to factor (h) the breadth of the claims, the Examiner contends that the claims are "fairly limited because they are drawn to filtering molecular descriptors using a **dynamic** filter." Inasmuch as the claims are not overly broad, Applicants submit this factor also supports a finding that the claimed invention is enabled.

The Examiner continues in her argument by saying that the specification "merely mentions the use of a **new** software developed by one of the inventors" without specific guidance. Presumably this is a reference to the passage at page 17, lines 19-24 which mentions the Multidyn software. However, as discussed hereinabove, the specification also has extensive and enabling passages at page 9, line 3 to page 10 line 22 and page 35, line 3 to page 37 line 23 which discuss dynamic filtering. Thus, even if the skilled artisan turned initially to the passage of the specification at page 17, lines 19-24, the skilled artisan could obtain further guidance from the rest of the specification at the cited passages. Thus, Applicants respectfully submit that the Examiner's

conclusion that the skilled artisan would have to turn to "trial and error experimentation" and, thus, undue experimentation is unfounded.

Inasmuch as each and every factor under the In re Wands test supports the finding that the instantly claimed invention is fully supported by the specification, Applicants assert the rejection under 35 U.S.C. §112, first paragraph for alleged lack of enablement is improper and respectfully request its withdrawal.

CLAIMS 1, 4, 5, 8-10, 18-20, AND 73 SATISFY THE REQUIREMENTS UNDER 35 U.S.C. §112, SECOND PARAGRAPH

Claims 1, 4, 5, 8-10, 18-20, and 73 have also been rejected under 35 U.S.C. §112, second paragraph for alleged indefiniteness. The Examiner contends that the metes and bounds of the term "dynamic filter" are unclear because there allegedly is "no description" of a dynamic filter in the specification.

Applicants submit that the passage at page 9, lines 3-20 clearly defines a dynamic filter as a "filter which employs one or more descriptors which characterize the dynamic behavior of a molecule," such as the "variation in the space occupied by a molecule over a period of time." Indeed, independent claims 1 and 18 recite that the dynamic filter represents "constraints of conformational variations which each candidate molecule must satisfy in order to exhibit [the] desired activity." Applicants also submit that, further in view of the arguments set forth hereinabove in support of the specification satisfying the written description and enablement requirements under 35 U.S.C. §112, first paragraph, a rejection based on the indefiniteness of the term "dynamic filter" can not be reasonably maintained.

Accordingly, Applicants respectfully request the withdrawal of the rejection of 1, 4, 5, 8-10, 18-20, and 73

under 35 U.S.C. §112, second paragraph for alleged indefiniteness.

CONCLUSION

In view of the amendments presented herewith, and the foregoing remarks, it is respectfully urged that the rejections set forth in the February 4, 2004 Official Action be withdrawn and that this application be passed to issue.

In the event the Examiner is not persuaded as to the allowability of any claim, and it appears that any outstanding issues may be resolved through a telephone interview, the Examiner is requested to telephone the undersigned attorney at the phone number give below.

Respectfully submitted,
DANN, DORFMAN, HERRELL AND SKILLMAN
A Professional Corporation

By _____
Donald R. Piper, Jr.
PTO Registration No. 29,337

Telephone: (215) 563-4100
Facsimile: (215) 563-4044
E-mail: dpiper@ddhs.com